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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,802	07/22/2003	Martin C. M. M. Barnardo	1181-282	5302

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
11/02/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/623,802	BARNARDO ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08/20/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-29,34-41,46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-29,34-41,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed August 20 2007 is acknowledged and has been entered.

Rejections Withdrawn

The written description rejection of claims 22-29, 34-41, 46 and 47 are withdrawn in view of applicant's arguments. However, the following rejections have been maintained.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 22-29, 34-41, 46 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of

working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method of depleting anti-major histocompatibility complex (anti-MHC) antibodies in a sample, wherein said anti-MHC antibodies are specific for a naturally occurring MHC allele, wherein the method comprises: a.) contacting eh sample with recombinant MHC or recombinant MHC-type molecules, wherein the recombinant MHC or recombinant MHC-type molecules are sufficiently antigenic to be bound by said anti-MHC antibodies in the sample, and wherein the recombinant MHC or recombinant MHC-type molecules comprise a class II heavy chain HLA monomer, a class II beta-2-microglobulin HLA monomer and a folding peptide; and b.) removing the bound anti-MHC antibodies from the sample, whereby the sample has been depleted of anti-MHC antibodies.

The specification on page 2, lines 1-2 disclose that HLA class II molecules are coded for by the DR, DQ, DP, DO and DM regions. The specification on page 12, lines 10-12 discloses that the invention extends to class II MHC molecules. Especially preferably the MHC molecules are in monomeric form. The specification fails to provide any working examples of recombinant MHC comprising a class II heavy chain HLA monomer, a class II beta-2-microglobulin HLA monomer and a folding peptide. The specification provides guidance on recombinant MHC class I molecules but does not provide guidance for MHC Class II molecules as claimed and as indicated in applicants specification MHC class I and MHC class II have completely different structures and different functions (see page 1 of the specification). Further, the synthesis of class II

MHC monomers at the time of the invention was not well known in the art. Barnardo et al (Transplantation, Vol 70, 531-536, No. 3, August 15, 2000) teaches that the synthesis of class II monomer is not well known and that success of an assay would depend on successful construction of these molecules (p. 536). Thomas et al (US 6,727,070) teaches that many proteins when produced recombinantly, suffer from improper processing, folding and lack normal solubility. Frayser et al (Protein Expression and Purification 15, 105-114, 1999) teaches that recombinant complexes of class II MHC proteins with single, defined peptides or empty, peptide-free molecules have met with limited success and that they suffer from chemical and physical heterogeneity and/or low yield (p. 105). Arimilli et al (The Journal of Biological Chemistry, Vol 270, No. 2, pp. 971-977, 1995) teaches that recombinant MHC class II molecules have difficulty in folding (p. 971). Therefore, one of ordinary skill in the art would have a low level of predictability in making MHC class II monomers that present a unique epitope of a naturally occurring MHC allele and binds to anti-MHC antibodies that are specific for the naturally occurring MHC allele. At best, one of skill in the art would have to perform random experimentation to try and construct a recombinant MHC Class II monomer that would function as claimed and random experimentation is undue.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 22-29, 34-41, 46 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 the recitation "recombinant MHC-type molecules" is vague and indefinite. It is unclear what applicant intends. Applicant has not provided a definition for the term and it is unclear what is considered to be a MHC-type molecule. See deficiencies throughout the claims.

Claim 22 the recitation "folding peptide" is vague and indefinite. Applicant does not provide a definition for the term "folding peptide" nor does the specification disclose the term "folding peptide" anywhere within the specification. Further, it is unclear if the peptide is folded or if the peptide would cause the recombinant MHC molecule to fold. It is unclear what applicant intends to encompass.

Claim 36 the recitation "recombinant HLA-type molecules" is vague and indefinite. It is unclear what applicant intends. Applicant has not provided a definition for the term and it is unclear what is considered to be a HLA-type molecule. See deficiencies throughout the claims.

Response to Arguments

5. Applicant's arguments filed August 20, 2007 have been fully considered but they are not persuasive.

112 Enablement Rejection

Applicant states that the state of the art at the time of filing, the Office Actions states that "the synthesis of class II MHC monomers at the time of the invention was not well known in the art (pages 4-5 of office action of 20 Feb 2007). Applicant states that however, the office action of 6 July 2006 cited US 6,232,445 as disclosing "recombinant MHC class II molecules, Thus, by the Office's own admission, recombinant MHC class

II molecules were part of the state of the art at the time of filing. This is not found persuasive because as stated above and in the previous office action the state of the prior art of the synthesis of class II MHC monomers is not well known. Further, it is noted that applicant has failed to address the state of the art presented by the Examiner above and in the previous office action. Particularly, the teachings of Barnardo et al which teaches that the synthesis of class II monomer is not well known and that success of an assay would depend on the successful construction of these molecules. Further, the teachings of Thomas et al., Frayser et al and Arimilli et al show of the difficulties and unpredictability of producing recombinant MHC molecules.

Applicant further argues that the Office Action provides no evidence as to why well-known recombinant techniques could not be used to generate MHC class II monomers. This is not found persuasive because of reasons of record and further as shown above the state of the art teaches that the synthesis of class II MHC monomers are not well known in the art and the state of the art also teaches of the unpredictability and difficulty of producing recombinant MHC molecules.

Applicant further argues that the examiner's interpretation of the claims, the recombinant MHC molecules should be produced to preserve epitopic sites, rather than generate "unique epitopes". This is not found persuasive because the Examiner has not stated that the epitiope is generated but rather that the recombinant molecule presents a unique epitope. Applicant further states that the identical issue was recently discussed in the parent application to the present application, United States Serial No. 09/809,029. This is not found persuasive because the methods of the different

applications are different methods and each case is treated individually and on its own merits further, the claims in 09/809,029 did not require the specifics of the current application. Particularly recombinant class II MHC monomers comprising a heavy chain HLA monomer, a class II beta-2-microglobulin HLA monomer and a folding peptide.

112 2nd rejections

Applicant argues that "HLA-type molecules" are molecules that exhibit properties of an HLA molecule ("HLA-type"). This is not found persuasive because of reasons of record and further because it is unclear what properties applicant is referring to.

Applicant argues that the recitation "folding peptide" is not vague and indefinite. Applicant argues that the specification is replete with examples of monomers that were folded around peptides and directs the Examiner's attention to paragraph 0074 of US 2004/0191245. This is not found persuasive because of reasons stated above and further, limitations from the specification are not read into the claims and the claims must stand on their own merits and as stated above it is unclear if the peptide is folded or if the peptide would cause the recombinant MHC molecule to fold.

Conclusion

6. No claims are allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
Examiner
Art Unit 1641
October 17, 2007

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